



Thursday, Feb 26, 2004

## **FDA Approves Avastin, A Targeted Therapy for First-Line Metastatic Colorectal Cancer Patients**

**SOUTH SAN FRANCISCO, Calif. -- February 26, 2004** — Genentech, Inc. (NYSE: DNA) announced today that the U.S. Food and Drug Administration (FDA) has approved Avastin™ (bevacizumab) to be used in combination with intravenous 5-Fluorouracil-based chemotherapy as a treatment for patients with first-line or previously untreated metastatic cancer of the colon or rectum. Avastin is the first FDA-approved therapy designed to inhibit angiogenesis, the process by which new blood vessels develop, which is necessary to support tumor growth and metastasis. Genentech will begin shipping Avastin within three calendar days.

The Avastin FDA approval is based on data from two trials. The pivotal trial was a large, placebo-controlled, randomized study that demonstrated a prolongation in the median survival of patients treated with Avastin plus the IFL (5-FU/Leucovorin/CPT-11) chemotherapy regimen by approximately five months, compared to patients treated with the IFL chemotherapy regimen alone (20.3 months versus 15.6 months). In addition, this study demonstrated an improvement in progression-free survival (PFS) of more than four months (10.6 months in the Avastin/IFL arm compared to 6.4 months in the IFL-alone arm). The survival and PFS results observed when Avastin is added to first-line chemotherapy are the longest ever reported in a randomized, Phase III study of patients with metastatic colorectal cancer.

In the pivotal trial, the most serious adverse events that occurred with Avastin included gastrointestinal perforations and wound healing complications, which were uncommon. The most common severe adverse events in this trial included hypertension, which was managed with oral medications, nosebleeds and asymptomatic proteinuria. Adverse events observed in other trials with Avastin included hemorrhage, congestive heart failure and thromboembolism.

"Today marks an important shift in the treatment of metastatic colorectal cancer, with the approval of an innovative treatment based on elegant science that targets cancer in an entirely new way," said Arthur D. Levinson, Ph.D., Genentech's chairman and chief executive officer. "The FDA's approval of Avastin would not have been possible without the dedication and passion of hundreds of Genentech employees, clinical trial investigators, patient advocates, the FDA and, most importantly, all of the colorectal cancer patients and their families who volunteered for Avastin clinical trials. We're pleased that patients diagnosed with metastatic colorectal cancer today have a new treatment option."

"When I was diagnosed with Stage Four colorectal cancer, my first thought was of my family and whether there were any treatments that could help me," said Earl Woodard, a commercial airline pilot from Carthage, N.C. "I received Avastin in the Phase III clinical trial. I am not only excited to have benefited from Avastin and chemotherapy, but it is also a great feeling to have participated in a clinical trial that has led to a new drug being approved for patients with metastatic colorectal cancer."

### **About the Avastin Filing**

The Avastin filing was submitted under the FDA's Fast Track program, which permits submission of documents on an ongoing or "rolling"-basis to facilitate the review process. Genentech submitted the final documents for the Avastin Biologics License Application (BLA), which contained data from more than 1,400 patients who received treatment with Avastin in clinical trials, in September 2003. In November 2003, the FDA granted Priority Review status for Avastin and committed to reviewing the submission within six months of filing.

"Every nine minutes someone in the United States dies of colorectal cancer. As a patient advocate, I understand the desperate need for new therapies for patients with this disease," said Kevin Lewis, board chairperson of the Colon Cancer Alliance.

### **About the Avastin Pivotal Trial**

The Avastin pivotal trial enrolled 925 patients with first-line (previously untreated) metastatic colorectal cancer, which is cancer that has spread beyond the colon or rectum. This trial was designed with a primary endpoint of survival and compared survival of patients treated with Avastin plus the IFL chemotherapy regimen to those treated with IFL chemotherapy and placebo. In addition to showing an improvement in

survival in all patient populations studied, the trial also met its secondary endpoints by improving progression-free survival, response rate and duration of response.

#### **About VEGF and Tumor Angiogenesis**

The link between angiogenesis and cancer growth has been discussed by many researchers for decades. It wasn't until 1989 that a key growth factor influencing the process, Vascular Endothelial Growth Factor (VEGF), was discovered by Napoleone Ferrara, M.D., a staff scientist at Genentech. Dr. Ferrara and his team cloned VEGF, providing some of the first evidence that a specific angiogenic growth factor existed. This research was published in the journal *Science* in 1989. Dr. Ferrara then created a mouse antibody to this protein. In 1993, Dr. Ferrara and his team at Genentech, in a study published in *Nature*, demonstrated that the antibody directed against VEGF could suppress angiogenesis and tumor growth in preclinical models, providing compelling evidence that VEGF can play a critical role in tumor growth. Clinical studies with a humanized version of the antibody, Avastin, began in 1997.

"Since the pivotal trial results were presented last year, I have had the privilege of meeting several patients who have received treatment with Avastin, and this has been the most rewarding part of watching a scientific theory progress from the lab to the clinic," said Dr. Ferrara. "The approval of Avastin is a testament to the many scientists both within Genentech and around the world who have worked tirelessly, even in the face of adversity and skepticism, to contribute to our understanding of angiogenesis and VEGF."

"Dr. Ferrara's scientific accomplishments and the approval of Avastin mark a turning point in science as it proves the long-pursued angiogenic hypothesis and, through an elegantly designed clinical trial, has turned a theory into a treatment for metastatic colorectal cancer patients," said Judah Folkman, M.D., professor of pediatric surgery at Children's Hospital and Harvard Medical School.

#### **About Avastin**

Avastin is a therapeutic antibody designed to inhibit VEGF, a protein that plays an important role in tumor angiogenesis and maintenance of existing tumor vessels. By inhibiting VEGF, Avastin is designed to interfere with the blood supply to a tumor, a process that is critical to a tumor's growth and metastasis. For full prescribing information and boxed warnings on Avastin and information about angiogenesis, visit <http://www.gene.com>. For more information on Avastin, visit [www.avastin.com](http://www.avastin.com).

Based on data showing that VEGF may play a broad role in a range of cancers, Genentech is pursuing a late-stage clinical development program with Avastin evaluating its potential use in metastatic colorectal, renal cell (kidney), breast and non-small cell lung cancers. Avastin is also being evaluated in earlier stage trials as a potential therapy in prostate, ovarian, melanoma and several types of solid tumor cancers and hematologic malignancies.

#### **About Colorectal Cancer**

According to the American Cancer Society, more than 150 patients die every day from colorectal cancer in the United States. Colorectal cancer is the second leading cause of cancer death in the United States, the third most frequently diagnosed cancer, and approximately 147,000 new cases of colorectal cancer will be diagnosed in the United States in 2004.

#### **About Genentech BioOncology**

Genentech is committed to fundamentally changing the way cancer is treated by establishing a broad oncology portfolio of innovative, targeted therapies that can improve patients' lives. Led by Rituxan® (Rituximab) and Herceptin® (Trastuzumab), the first two therapeutic antibodies approved to treat cancer in the United States and Avastin™ (bevacizumab), the first anti-angiogenic therapy approved to treat cancer in the United States, the BioOncology portfolio includes marketed and pipeline products in clinical trials for the seven most common lethal cancers.

Genentech has a robust pipeline of potential oncology therapies, including a small molecule designed to target the human epidermal growth factor receptor (HER1) pathway (also known as EGFR) and a therapeutic antibody directed at the HER pathway. To broaden Genentech's portfolio of targeted cancer therapies, research programs are leveraging Genentech's expertise in targeting additional components of the HER and angiogenesis pathways, as well as pathways that instruct cancer cells to die (i.e., apoptosis), and B-cell oncology.

#### **About Genentech**

Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes

biotherapeutics for significant unmet medical needs. Eighteen of the currently approved biotechnology products originated from or are based on Genentech science. Genentech manufactures and commercializes 13 biotechnology products in the United States. The company has headquarters in South San Francisco, California and is traded on the New York Stock Exchange under the symbol DNA. For additional information about the company, please visit <http://www.gene.com>.

Genentech will be offering a live webcast of a discussion by Genentech management on Thursday, February 26, 2004 at 3:00 p.m. PT. The live webcast may be accessed on Genentech's website at <http://www.gene.com>. An archive of this webcast will be available until 5:00 p.m. PT on March 4, 2004. An audio replay of the webcast will be available beginning at 6:00 p.m. PT on February 26, 2004, through 5:00 p.m. PT on March 4, 2004. Access numbers for this replay are: 1-800-642-1687 (US/Canada) and 1-706-645-9291 (international); conference identification number is 5855709.

# # #

For full prescribing information for Avastin, please call 650-225-7739 or visit <http://www.gene.com>.

© Genentech, Inc.